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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/584,982	04/02/2007	Robin Kurfurst	15675P620	2408

7590 09/26/2011

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EXAMINER	
GIBBS, TERRA C	
ART UNIT	PAPER NUMBER
1635	
MAIL DATE	DELIVERY MODE
09/26/2011	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/584,982	KURFURST ET AL.	
	Examiner	Art Unit	
	TERRA C. GIBBS	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 September 2011*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

5)☒ Claim(s) *38,42,46-57 and 60-66* is/are pending in the application.

5a) Of the above claim(s) _____ is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☒ Claim(s) *38,42,46-57 and 60-66* is/are rejected.

8)☐ Claim(s) _____ is/are objected to.

9)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

10)☐ The specification is objected to by the Examiner.

11)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

12)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *See Continuation Sheet*.

Continuation of Attachment(s) 6). Other: attached sequence alignment and original sequence for SEQ ID NO:4.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission mailed on September 13, 2011 has been entered.

Claims 43-45 have been canceled.

Claims 38, 42, 46-53, 55, and 57 have been amended.

Claims 38, 42, 46-57, and 60-66 are pending in the instant application.

Claims 38, 42, 46-57, and 60-66 have been examined on the merits.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Response to Arguments

Applicant's Amendment and Response filed September 13, 2011 have been considered. Rejections and/or objections not reiterated from the previous Office Action mailed March 14, 2011 are hereby withdrawn. Any arguments addressing said rejections and/or objections are moot. The following rejections and/or objections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application.

Claim Rejections - 35 USC § 103

In the previous Office Action mailed March 14, 2011, claims 38, 42-57, and 60-67 were rejected under 35 U.S.C. 103(a) as being unpatentable over WO 95/02069 A1, also referred to as "Bennett" (submitted and made of record on Applicant's Information Disclosure Statement filed November 20, 2006) in view of Park et al. (Journal of Biological Chemistry, 1993 Vol. 268:16:11742-11749, submitted and made of record on Applicant's Information Disclosure Statement filed November 20, 2006). **This rejection is moot** against claims 43-45 in view of Applicant's Amendment filed September 13, 2011 to cancel these claims. **This rejection is maintained** against claims 38, 42, 46-57, and 60-66 for the reasons of record set forth in the previous Office Action mailed March 14, 2011.

Response to Arguments

In response to this rejection, Applicants argue that in regard to independent claims 38 and 57, Bennett in view of Park fails to disclose or render predictable a method of depigmenting or bleaching human skin, body hair or hair of a head including an oligonucleotide having SEQ ID NO:4 as required by claims 38 and 57.

This argument has been considered, but is not found persuasive because Bennett disclose and claim a method of treating a condition associated with expression of PKC comprising administering to a mammal a therapeutically effective amount of an oligonucleotide specifically hybridizable with a PKC gene or mRNA. See claim 70. Bennett also discloses and claims that the condition associated with the expression of

PKC is a hyperproliferative disorder being psoriasis. See claims 71 and 72. Bennett also discloses and claims that the PKC gene is specifically PKC beta-1 (see claims 85, 89, and 90 and SEQ ID NOs: 25-29, particularly SEQ ID NO:27).

Furthermore, and as noted in the previous Office Action mailed June 16, 2010 at pages 7 and 8, it is noted that Bennett do not explicitly teach that the topical administration of antisense oligonucleotides targeted to PKC beta-1 will result in a method of depigmenting or bleaching human skin. However, Applicant is reminded that the burden of establishing whether the teachings of Bennett would have the additional function of resulting in a depigmenting effect, under generally any assay conditions falls to Applicant. See MPEP 2112.02.

Regarding Applicant's arguments concerning an oligonucleotide having SEQ ID NO:4, Bennett indeed teach an oligonucleotide having SEQ ID NO:4 of Applicant's claimed invention. See attached sequence alignment.

Applicants next argue that Applicants do not believe Bennett or Park disclose an oligonucleotide having SEQ ID NO:4. Applicants argue that Bennett discloses SEQ ID NO:27, which does not appear to be the same as SEQ ID NO:4 of Applicant's invention.

This argument has been considered, but is not found persuasive because according to the current sequence listing, SEQ ID NO:4 of Applicant's claimed invention is: gccagcatgt gcaccgtgaa. SEQ ID NO:27 of Bennett is gccagcatgt gcaccgtgaa. Furthermore, SEQ ID NO:27 of Bennett aligns perfectly with SEQ ID NO:4 of Applicant's invention, and without any mismatches. See attached sequence alignment.

It is noted that in Applicant's arguments filed September 13, 2011, at page 8, Applicants contend that SEQ ID NO:4 of Applicant's invention is: GCC AGG AT**C** TGC ACC GTG AA. However, this sequence is incorrect as the correct sequence of SEQ ID NO:4 accordingly to the current sequence listing is GCC AGC AT**G** TGC ACC GTG AA. Thus, Applicant's arguments regarding the sequence of SEQ ID NO:4 of Applicant's claimed invention as it relates to SEQ ID NO:27 of Bennett is misplaced as it appears that Applicants are reciting a sequence that does not match to what is currently listed in the sequence listing of record. Applicant is also invited to view the original sequence listing filed June 29, 2006, where SEQ ID NO:4 is listed as gccagcatgt gcaccgtgaa, and not GCC AGG AT**C** TGC ACC GTG AA as Applicants contend. See attached.

Applicants next argue that Bennett teaches that, for the treatment of a particular disease, one of ordinary skill in the art should use oligonucleotides specific for one or more PKC isoforms that are known to be associated with that particular disease. That is, Bennett teach that specific oligonucleotides should be used depending on the knowledge concerning which PKC isoforms(s) is/are associated to a particular disease.

This argument has been fully considered, but is not found persuasive because Bennett teach oligonucleotides targeted to both PKC beta 1 and PKC beta-2 (Table 2); oligonucleotides targeted to PKC beta 1 only (Table 3); and oligonucleotides targeted to PKC beta 2 only (Table 4). Furthermore, Bennett also disclose and claim a method of treating a condition associated with expression of PKC comprising administering to a mammal a therapeutically effective amount of an oligonucleotide specifically hybridizable with a PKC gene or mRNA. See claim 70. Bennett also discloses and

claims that the condition associated with the expression of PKC is a hyperproliferative disorder being psoriasis. See claims 71 and 72. Bennett also discloses and claims that the PKC gene is specifically PKC beta-1 (see claims 85, 89, and 90 and SEQ ID NOs: 25-29, see particularly SEQ ID NO:27).

Furthermore, and as noted in the previous Office Action mailed June 16, 2010 at pages 7 and 8, it is noted that Bennett do not explicitly teach that the topical administration of antisense oligonucleotides targeted PKC beta-1 will result in a method of depigmenting or bleaching human skin. However, Applicant is reminded that the burden of establishing whether the teachings of Bennett would have the additional function of resulting in a depigmenting effect, under generally any assay conditions falls to Applicant. See MPEP 2112.02.

Applicants next argue that it is clear from the global teachings of Bennett that oligonucleotides of Table 3 should be used for "diseases associated to PKC beta-1 only". Yet, Bennett does not disclose any disease associated to PKC beta-1 only, let alone melanogenesis-linked diseases. Applicants contend that the Examiner has not identified a document disclosing that melanogenesis-linked diseases are PKC beta-1 only associated diseases. Applicants argue that Park, on the other hand, refers to PKC beta in general and suggests that both PKC beta-1 and PKC beta-2 are involved in melanogenesis. Applicants argue that this fact is also supported by the teachings of Nishizuka et al. (made of record on December 14, 2010). Applicants contend that they have found that the specific targeting of only PKC beta-1 is sufficient to inhibit melanogenesis and this effect is not taught nor suggested by any of the cited art.

This argument has been fully considered, but is not found persuasive because Bennett disclose and claim a method of treating a condition associated with expression of PKC comprising administering to a mammal a therapeutically effective amount of an oligonucleotide specifically hybridizable with a PKC gene or mRNA. See claim 70. Bennett also discloses and claims that the condition is a hyperproliferative disorder being psoriasis. See claims 71 and 72. Bennett also discloses and claims that the PKC gene is specifically PKC beta-1 (see claims 85, 89, and 90 and SEQ ID NOs: 25-29, se particularly SEQ ID NO:27).

As noted in the previous Office Action mailed June 16, 2010 at pages 7 and 8, it is noted that Bennett do not explicitly teach that the topical administration of antisense oligonucleotides targeted PKC beta-1 will result in a method of depigmenting or bleaching human skin. However, Applicant is reminded that the burden of establishing whether the teachings of Bennett would have the additional function of resulting in a depigmenting effect, under generally any assay conditions falls to Applicant. See MPEP 2112.02.

Furthermore, by using the method steps disclosed by Bennett, it is the Examiner's position that a method of depigmenting or bleaching human skin as instantly claimed would necessarily flow from the teachings of Bennett, absent evidence to the contrary. See MPEP 2112.02. This is primarily due to the fact that the method steps of Bennett are the exact method steps of Applicant's claimed invention, being the administration of an oligonucleotide specifically hybridizable to PKC beta-1 and modifying expression of only PKC beta-1. Therefore, the methods of Bennett will

necessarily carry out the functionality of Applicant's claimed invention, absent some evidence to the contrary.

While it is noted that Park only refers to PKC beta, without indicating which isoform of PKC beta has been tested, and Park refers to PKC beta in general and suggests that both PKC beta-1 and PKC beta-2 are involved in melanogenesis, Bennett teaches a method of treating a condition associated with PKC beta expression comprising topically administering an oligonucleotide that specifically hybridizes with PKC beta. See claim 70 and page 18, lines 6-9. Bennett goes on to teach that the oligonucleotide that specifically hybridizes with PKC beta is specific for PKC beta-1 only. See Table 3 at SEQ ID NOs: 25-29, particularly SEQ ID NO:27.

As discussed *supra*, by using the method steps disclosed by Bennett, a method of depigmenting or bleaching human skin as instantly claimed would necessarily flow from the teachings of Bennett, absent evidence to the contrary. See MPEP 2112.02. Thus, the Examiner maintains her position that the method steps of Bennett are the exact method steps of Applicant's invention, namely the administration of an oligonucleotide specifically hybridizable to PKC beta-1 and modifying expression of only PKC beta-1. Therefore, the methods of Bennett will necessarily carry out the functionality of Applicant's claimed invention, absent some evidence to the contrary.

It should be noted that Bennett clearly motivated one of ordinary skill in the art to inhibit both PKC beta-1 and PKC beta-2 (Table 2); PKC beta-1 alone (Table 3); or PKC beta-2 alone (Table 4). Thus, Bennett provided the motivation to inhibit one PKC isoform over another. Therefore, one of skill in the art would have applied the teachings

and motivation provided by Bennett to arrive at Applicant's claimed invention of inhibiting only PKC beta-1, absent some evidence to the contrary. Thus, the specific targeting of PCK beta-1 is not novel since Bennett provided clear and explicit motivation for one of ordinary skill in the art to do so.

Furthermore, the specific targeting of PKC beta-1 to inhibit melanogenesis is not novel because the single method step involved for such inhibition is taught by Bennett and therefore the methods of Bennett will necessarily carry out such functionality, absent evidence to the contrary. See MPEP 2112.02.

In view of the foregoing, when all the evidence is considered, the totality of the rebuttal evidence of non-obviousness fails to outweigh the evidence of obviousness made of record. Thus, it is maintained that the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was filed.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Terra C. Gibbs whose telephone number is 571-272-0758. The examiner can normally be reached from 8 am - 5 pm M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Heather Calamita can be reached on 571-272-2876. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

September 22, 2011
/Terra Cotta Gibbs/
Examiner, Art Unit 1635